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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/185,908	11/03/98	BLASCHUK	1000086.49

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EXAMINER	
DECLOUX, A	
ART UNIT	**PAPER NUMBER**
1644	11

DATE MAILED: 06/30/00

Please find below and/or attached an Office communication concerning this application r proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/185,908	Blaschuck et al
Examiner	**Group Art Unit**
DeCloux, Amy	1644

☒ Responsive to communication(s) filed on *Apr 13, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-20, 27-43, 46-49, 52-55 and 58-61* is/are pending in the applicat

Of the above, claim(s) *9-10 and 14--20* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-8, 11-13, 27-43, 46-49, 52-55, and 58-61* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's election of Group I, claims 1-20, 27-43, 46-49, 52-55 and 58-61 in Paper No. 10, mailed April 10, 2000, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement of the groupings, the election has been treated as without traverse.

Applicant's election of species with traverse is noted. The traversal is on the ground(s) that the Examiner's search of all species in the elected claims does not create an undue burden, and that the recited peptides species contain specific non-critical flanking amino acids. However, it is not clearly the number and composition of amino acids that comprise a claudin CAR sequence. Additionally, it is noted that there are literally hundreds of peptide species recited in the instant claims, each with a distinct structure and accompanying characteristics. Because a search of hundreds of species would not be co-extensive with a search of the others, and because each species is a distinct biochemical structure, and for the reasons of record, an examination and search of all the recited species in a single application would constitute a serious undue burden on the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9-10, and 14-20 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10, mailed April 10, 2000.

It is also noted that the amendment to Claim 20 does not appear to change the claim in any way.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-4 and their dependent claims 5-8, 11-13, 27-43, 46-49, 52-55 and 58-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-4 and their dependent claims 5-8, 11-13, 27-43, 46-49, 52-55 and 58-61 are drawn to a cell adhesion modulating agent that comprises a claudin CAR sequence and contains as few as 3 amino acids and as many 50 amino acid residues. However, the specification does not enable one of skill in the art regarding how to make and use the agent. Applicant has generated this deduced consensus amino acid sequence for a claudin CAR sequence (SEQ ID NO:1), based on a sequence homology alignment of the amino acid sequences of extracellular domain one of representative mammalian claudins as indicated in Figure 1 of the instant specification. Applicants have disclosed that an agent comprising said claudin CAR sequence is capable of modulating claudin-mediated processes, such as cell adhesion, (see page 14, lines 10-21 of the instant specification). However; there is no clear guidance from Applicant's specification that an agent comprising SEQ ID NO:1 is capable of modulating claudin-mediated processes, such as cell adhesion, because applicant has not disclosed the sequence identity of CAR containing peptides that actually reduce cell adhesion in the disclosed example, nor the 9 amino acid CAR sequence used to make the antibodies that have cell adhesion modulating activity as disclosed in Examples 2 and 4. The only proposed uses for the an agent comprising the claimed CAR sequence are based upon an alignment with other mammalian claudins, and there is no predictability that this small sequence identity (or which part(s) thereof) would confer the biological activities including modulating claudin-mediated processes, such as cell adhesion, to an agent comprising the claimed CAR sequence (SEQ ID NO:1) because Applicant has not disclosed where the biological activity of cell adhesion of the claudin resides within the (SEQ ID NO:1 .

Furthermore, there is no clear guidance from Applicant's specification of the minimum number of amino acids from the deduced consensus amino acid sequence for a claudin CAR sequence (SEQ ID NO:1) is necessary to modulate claudin-mediated processes, such as cell adhesion. For example claim 1 recites that said agent comprises a claudin CAR sequence and contains 3-16 amino acids linked by peptide bonds, and claims 5 and 6 recites an agent of a peptide from 3-50 and 4-16 amino acid residues, respectively. Applicants disclose the deduced consensus amino acid sequence for a claudin CAR as having the sequence of SEQ ID NO:1 which contains 8 amino acids, and of those 8 amino acids, three can be any

amino acid. However, there is no clear guidance from Applicant's specification that an agent containing a three amino acid sequence where only the first amino acid is defined as being an Arg or a Lysine, as defined by SEQ ID NO:1, is capable of modulating claudin-mediated processes, such as cell adhesion. Similarly claims 2 and 3 recite a minimum of 5 or 7 consecutive amino acid residues SEQ ID NO:1, and there is no clear guidance from Applicant's specification that an agent of only 5 or 7 amino acids is capable of modulating claudin-mediated processes, such as cell adhesion. Based upon the paucity of information contained within the instant specification in this regard, and within the art at the time the invention was made, it would require an undue amount of experimentation on the part of one skilled in the art to use the claimed polypeptide for the asserted utilities. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Furthermore, there is no clear guidance from Applicant's specification what the effect of cyclization of a claudin CAR sequence will have on it cell adhesion functions. It is known in the art that even single amino acid in a protein's amino acid sequence can have dramatic effects on the protein's function. Since the amino acid sequence of a polypeptide determines its structural, immunogenic and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality requires detailed knowledge of the ways in which a polypeptide's structure relates to its function. In view of the insufficient guidance in the prior art and in applicants disclosure of the effect of cyclization of a claudin CAR sequence on its functions including cell adherence, making and using the claimed agent is complex and well outside the realm of routine experimentation.

In view of the quantity of experimentation necessary to use the claimed invention, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

4. Claims 1-4 and their dependent claims 5-8, 11-13, 27-43, 46-49, 52-55 and 58-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventor(s), at the time the application was filed, had possession of the

claimed invention. The instant claims are drawn to a cell adhesion modulating agent , comprising a claudin CAR sequence, which is disclosed as comprising a consensus sequence of 8 amino acids (SEQ ID NO:1), of which three amino acids are "independently selected". However, it is not clear from the disclosure, exactly which amino acids can be included in the group of "independently selected" amino acids and still comprise a claudin CAR sequence. It is not clear from the disclosure whether the independently selected amino acids must be present in an equivalent position as one of the sequences used to derive the claudin CAR consensus, or if other sequences may be substituted. Nor is it clear the minimum length of a claudin CAR sequence. Since only a consensus sequence of ambiguous length and sequence composition is disclosed, a claudin CAR sequence is not adequately described. Applicant has not adequately described what sets apart claudin sequences as a genus from sequences which are not claudin sequences.

5. Claims 33-34 and 38-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the CAR Sequence of the cell adhesion molecules as disclosed on page 48, lines 19-21, page 52, lines 9-12, page 53 lines 1-3 and page 61, lines 7-12 (encompassing SEQ ID NO:s 25 and 26), and for agent comprising an antibody or antigen-binding fragment thereof, does not reasonably provide enablement for a cell adhesion modulating agent comprising <u>any</u> cell adhesion recognition sequence, known or unknown, that is bound by <u>any</u> adhesion molecule, known or unknown, other than those disclosed in the instant specification, nor an antibody or antigen binding fragment that specifically binds <u>any</u> cell adhesion recognition sequence that is bound by <u>any</u> adhesion molecule , other than those disclosed in the instant specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the large number of cell adhesion molecules, known and unknown, including any number of other extracellular matrix proteins as recited in claim 34 and broadly encompassed by the instant claims. Besides SEQ ID NO:1, 25 and 26, and those disclosed in the specification as mentioned above, the specification fails to

provide any guidance regarding any other specific sequence defining any cell adhesion recognition sequence that is bound by any adhesion molecule other than those disclosed in the instant specification. Based upon the paucity of information contained within the instant specification in this regard, it would require an undue amount of experimentation on the part of one skilled in the art to make or use an agent comprising any cell adhesion recognition sequence, known or unknown, that is bound by any adhesion molecule, known or unknown, other than a claudin and those disclosed in the instant specification, nor an antibody or antigen binding fragment thereof that specifically binds to any cell adhesion recognition sequence that is bound by any adhesion molecule other than a claudin and those disclosed by the instant specification, for the asserted utilities including modulating cell adhesion.

In view of the quantity of experimentation necessary to use the claimed invention, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

7. Claims 2-7 and 27-39 are rejected under *35 U.S.C. § 112*, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

A) Claims 27-39 are indefinite for being dependent upon claims 24-26, which have been canceled.

B) Claim 33 is indefinite in the recitation of the phrase "...sequence that is bound by an adhesion molecule..." because it is not clear how a molecule can bind to a sequence.

C) Claims 5 and 6 are indefinite in the recitation of an agent is a peptide ranging in size from 3 to 50 amino acid residues or from 4-50 amino acid residues, respectively, since claims 2, 3 and 4 encompass 5, 7 and 8 consecutive amino acid residues of SEQ ID NO:1, respectively.

D) Claims 2-7 are indefinite in their recitation of the phrase "independently

selected amino acid residues" because it is not clear which specific amino acids are encompassed by said phrase.

8. The following is a quotation of the appropriate paragraphs of *35 U.S.C. § 102* that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-3, 5-7 and 35 are rejected under 35 U.S.C. 102(b) as anticipated by Ruoslahti et al (U.S. Patent No.5,627,263, May 6, 1997).

Ruoslahti et al teach the nonomer sequence an amino acid sequence CRGDSFVGC (see entire article, including Figure 3) comprising at least 5 and 7 consecutive amino acids of SEQ ID NO:1. Therefore, the referenced teachings anticipate the claimed invention.

10. Claims 2, 35 and 40 are rejected under 35 U.S.C. 102(b) as anticipated by Bult et al. (Science 273:1058-1073, 1996).

Bult et al teach a 47mer protein that comprises the sequence IYSYX (see entire article) comprising at least 5 consecutive amino acids of SEQ ID NO:1. Therefore, the referenced teachings anticipate the claimed invention.

11. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-6, 7-8, 11-20, 27-40, 41-43 and 46-49 are provisionally rejected under

35 U.S.C. 101 as claiming the same invention as that of claims 1-6, 8-9, 10-19, 26-39, 41-43 and 46-49 of copending Application No. 09/282029. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy DeCloux whose telephone number is (703) 306-5821. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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June 30, 2000

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